CLAIMS

1. A method for local and superficial (probed volume and measuring area with dimensions on the order of one transport mean free path) characterization of a turbid medium using the following parameters:

1) the refractive index n of the turbid medium

2) the absorption coefficient μ_a of the turbid medium.

3) the reduced scattering coefficient μ_s' of the turbid medium.

4) the phase function parameter $\gamma=(1-g_2)/(1-g_1)$ of the turbid media, where g_1 and g_2 are the first two moments of the Legendre polynomial development of the phase function p,

and comprising the steps of:

- measuring the spatially-resolved reflectance $R(\rho)$of the turbid medium (ρ being the source-detector distance) by any mean, comprising an illumination beam as a source and an optical detector, which, by using optional signal processing, which may involve filtering and de-convolution operation to correct for the non-zero area of either the illumination source or the detector, allows for the precise determination of the said spatially-resolved reflectance $R(\rho)$,
- mathematically processing $R(\rho)$ to compute at least one of the said parameters: n, μ_a ,, μ_s', γ and/or the variations, in time and/or space, of at least one of the said parameters: Δn, $\Delta\mu_a$, $\Delta\mu_s'$, $\Delta\gamma$, whereby the said "inverse problem", which consists in extracting the optical coefficients from the spatially resolved

reflectance data is solved, and whereby the said "direct problem" consists in computing the spatially resolved reflectance from the values of the optical coefficients n, μ_a, μ_s', γ involved in a model of propagation of the light in turbid medium and whereby the said "model" incorporates a Legendre polynomial development to the second order of the said "phase function", and whereby the said "phase parameter" γ is introduced in the computation as an independent parameter.

2. The method of claim 1, wherein said spatially resolved reflectance is measured by a probe comprising at least one optical fiber carrying the light from the source unit to the turbid medium and at least one optical fiber collecting the reflected light and carrying it to detection unit, whereby the combination of a variety of emitting fibers and of receiving fibers yields a set of distances ρ at which the reflectance $R(\rho)$ is measured.

3. The method according to any one of claims 1 and 2, wherein said spatially resolved reflectance $R(\rho)$ is measured for a set of values of ρ, by using a probe composed of optical fibers in any of the following configurations:

- one emitting optical fiber and a set of optical receiving fibers
- a set of optical emitting fibers and one optical receiving fiber
- a set of optical emitting fibers and a set of optical receiving fibers

giving the spatially resolved reflectance $R(\rho)$ at a variety of source – detector distance ρ. The emitting and receiving fibers can be arranged in a variety of configurations. In some particular arrangement they can be positioned:

- on a line,
- on crossed lines,
- on a circle,
- on an ellipse
- on crossed ellipses
- on a disk, a rectangle, or any surface, as a dense and contiguous arrangement of fibers, such as it can be obtained with a bundle of fibers or a multi-core fiber,
- on any pattern resulting from the combination of the above mentioned patterns.

4. The method according to any one of claims 1, 2 and 3, wherein said spatially resolved reflectance is measured by an optical and electronic micro-system comprising a collimated or focused beam as illuminating source and 1D or 2D arrays of optical detectors, arranged in a way similar to the one described in claim 3, and which, in some embodiment, can be a CCD or MOS camera.

5. The method according to any one of claims 1-4, where the probe of claims 2 and 3 or the optical and electronic micro-system of claim 4 are put in contact to the turbid medium.

6. The method of claim 1, wherein said spatially resolved reflectance is measured by a non-contact system, comprising at least one of the following combination of optical systems:

- a fixed optical system to irradiate the turbid medium with a collimated or focused beam forming the illuminating source and a fixed optical system comprising an imaging system forming the image of the measured area of the turbid medium on a said "optical detector", which can be formed of 1D or 2D array of optical detectors, whereby this second optical system can be identical to the first one and whereby the array of optical detectors can be either one of the following system:
    - a set of optical fibers arranged in a variety of configurations similar to those described in claim 3,
    - an optical and electronic micro-system (MOEM), which in some embodiment can be a CCD or MOS camera, with a functionality similar to the one described in claim 4,
- a fixed optical system for the collimated beam illuminating source and a scanned optical system for the said "optical detector",
- a scanning optical system for the collimated beam illuminating source and a fixed optical system for the said "optical detector",
- a scanning optical system for the collimated or focused beam used as an illuminating source and a scanning optical system for the said "optical detector".

7. The method according to any one of claims 1. to 6., wherein the absorption coefficient μ_a, the reduced scattering coefficient μ_s' and the phase function

parameter γ are determined by fitting the measured spatially-resolved reflectance $R(\rho, \mu_s', \mu_a, \gamma)$ to a set of discretized data obtained by using Monte Carlo simulations, or to interpolating functions giving a continuous approximation of the discretized data obtained by Monte Carlo simulations, and whereby said "Monte Carlo simulations" are based on a photon propagation model comprising a phase function approximated by a Legendre polynomial development limited to the second order. In a preferred embodiment, cubic splines are used as interpolating functions.

8. The method according to any one of claims 1 to 7, wherein the following signal processing steps can be performed in addition to the processing steps of any of the claims 1-6 whereby the processing of the spatially resolved reflectance data of claim 7 can be simplified and accelerated by:

- fitting the measured reflectance $R(\rho)$ by the function:

$$m_1\rho^{m_2}\exp(m_3\rho)$$

This fit gives the values of the parameters m_1, m_2 and m_3, assuming that the expression $R(\rho)=m_1\rho^{m_2}\exp(m_3\rho)$ gives a smoothed expression of the spatially resolved reflectance $R(\rho)$.

- Computing the slopes $\frac{\partial}{\partial\rho}\sqrt{R(\rho)}$ and $\frac{\partial}{\partial\rho}(\ln R(\rho))$, or any mathematical combinations of these two latter quantities and $R(\rho)$, from analytical functions using the parameters m_1, m_2 m_3, or by numerical procedures from the expression $R(\rho)=m_1\rho^{m_2}\exp(m_3\rho)$

- computing the values of at least one of the said parameters: n, μ_a, μ_s', γ and/or the variations, in time and/or space, of at least one of the said parameters: Δn, $\Delta\mu_a$, $\Delta\mu_s'$, $\Delta\gamma$ from the relationship between the reflectance intensity $R(\rho)$ and the slope of $\ln R(\rho)$ (denoted $\partial\rho \ln R$), determined at a fixed distance ρ comparable to the transport mean free path, whereby the computation is made from the data obtained by Monte Carlo simulations, provided that said "Monte Carlo simulations" are based on a photon propagation model comprising a phase function approximated by a Legendre polynomial development limited to the second order.

9. The method according to any one of claims 1 to 7, wherein the following signal processing steps can be performed in addition to the processing steps of any claim 1-6 whereby the processing of the spatially resolved reflectance data of claim 7 can be simplified and accelerated by:

- computing the reduced scattering coefficient μ_s' and the phase function parameter γ by using the following form of the reflectance:

$$R(\rho) = (A(\rho, \gamma, \mu_s') + B(\mu_a, \mu_s'))^2$$

where the function $A(\rho, \gamma, \mu_s')$ and $B(\mu_a, \mu_s')$ depend also on the sources and detectors characteristics, and the refractive index of the sample, and comprising the steps of:

- Computing the slopes of the square root of the spatially resolved reflectance $\frac{\partial}{\partial\rho}\sqrt{R(\rho,\mu_s',\mu_a,\gamma)}=\frac{\partial A}{\partial\rho}(\rho,\mu_s',\gamma)$, which depends weakly on the absorption coefficient μ_a for $0.3<\rho\mu_s'<5$, for at least two distances ρ,
- Determining the parameters μ_s' and γ by a polynomial interpolation of the data obtained by Monte Carlo simulations, whereby said "Monte Carlo simulations" are based on a photon propagation model comprising a phase function approximated by a Legendre polynomial development limited to the second order.

10. The method of claims 9, wherein the absorption coefficient μ_a is determined by using the equation:

$$\mu_a = h\left[\sqrt{R(\rho,\mu_s',\mu_a,\gamma)}-f(\gamma,\mu_s')\right]$$

where f and h are continuous functions of the parameters ρ, μ_s' and γ of that can be approximated by a polynomial interpolation of the data obtained by Monte Carlo simulations, whereby said "Monte Carlo simulations" are based on a photon propagation model comprising a phase function approximated by a Legendre polynomial development limited to the second order.

11. The method according to any one of claims 1 to 7, wherein the difference $\Delta\mu_a=\mu_a-\mu_{ao}$ between the absorption coefficient μ_a and a known value μ_{ao} is computed from the quantity $\sqrt{R(\rho,\mu_s',\mu_{a0},\gamma)}-\sqrt{R(\rho,\mu_s',\mu_a,\gamma)}$ = $B(a')$- $B(a_0')$, whereby the function $B(a')$ of the albedo a' can be can be approximated by a

polynomial interpolation of the data obtained by Monte Carlo simulations, whereby said "Monte Carlo simulations" are based on a photon propagation model comprising a phase function approximated by a Legendre polynomial development limited to the second order, and whereby the calculation can be done for a single γ value, because the influence of the phase function parameter and γ in $B(a')$ are particularly weak.

12. The method according to any one of claims 1 to 11, wherein the illuminating source is a broadband source or a white light source and the detector unit comprises a spectrograph or any wavelength analysis system to measure the wavelength dependence of at least one of the parameters $(n, \mu_a, \mu_s', \gamma)$.

13. The method according to any one of claims 1 to 12, wherein said turbid medium is a biological medium.

14. The method according to any one of claims 1 to 13, wherein the measurement and processing is repeated at different location of the sample (multi-site measurements), to build images of any one of the said parameters $(n, \mu_a, \mu_s', \gamma)$.

15. An apparatus using the method of claim 1 to 3, 5 or 7 to 14 for local and superficial characterization of a turbid medium,

a) comprising a source, a detection unit, reference means, signal processing means, a probe comprising at least one optical fiber connecting said source unit to the

turbid medium and at least one optical fiber connecting the turbid medium to the said detection unit, and reference means

b) where the distance between the source and the detector is close to one transport mean free path

16. An apparatus using the method of claim 1, 4, 5, or 7 to 14 for local and superficial characterization of a turbid medium,

a) comprising an optical and electronic micro-system comprising at least one illuminating source, at least one detector , signal processing means and reference means ,

b) where the distance between the source and the detector is close to one transport mean free path

17. An apparatus using the method of claim 1 or 6 to 14 for local and superficial characterization of a turbid medium,

a) comprising a collimated or focused beam used as an illuminating source, at least an optical detector for the detection unit, a fixed or scanning optical system for the illuminating source and a fixed or scanning optical system for the said "optical detector", signal processing means and reference means,

b) where the distance between the source and the detector is close to one transport mean free path

18. Three apparatus similar to the apparatus described in any one of the claims 15, 16 and 17 , and characterized by the fact that the distance between the collimated or focused optical beam used as illuminating source and the emitting point connected to an optical detector varies from 0.1 to 2mm. for application to biological media and to turbid media having a transport mean free path similar to biological media.

19. A test , where the control of the homogeneity of the sample over the probed area is performed with the apparatus of any one of the claims 15, 16,17 and 18 , which can be carried out according to the following optional procedure: In the apparatus two illuminating fibers are disposed symmetrically in regard to the collecting fibers. If the sample is homogeneous, the reflectance curve should be identical with either illuminating fiber. Therefore, heterogeneity of the investigated region or obstructions beneath the fibers are detected by comparing the two curves. If the two curves are sufficiently close, the measurement is validated and the average of the two curves is calculated.

20. A calibration and normalization procedure, which are carried out optionally with the apparatus of any one of the claims 15, 16,17 and 18 , whereby the following steps are performed:

1) In order to perform relative intensity measurements, the differences of transmitted intensity between each fiber for the apparatus of claim 15 or the differences of signal intensity between each optical detector for any of the claims 16 and 17, are determined by performing a measurement on a turbid

phantom illuminated uniformly or a diffusing sphere of perfectly uniform properties. In this calibration procedure, the background light, measured with the light source turned off, must be subtracted from the signal. The obtained values are used to multiply the measurements given by each fiber and/or detector to correct the relative intensity measurements.

2) In order to perform absolute intensity measurements, a calibration can be performed on a turbid medium of known optical properties, which can be realized according to any one of the following recipe:

a) solid or liquid turbid medium which properties have been measured by other techniques, or reported in the literature,

b) water suspension of micro-spheres of known size distribution and refractive index. Absorbing dye may be added to the suspension. In this case, the scattering properties are calculated from Mie theory, and the absorption coefficient is assumed to be equal to the water absorption coefficient, if no absorbing dye is added. If an absorbing dye is used, the absorption coefficient can be measured by a spectrophotometer, before mixing the solution with any scattering materials.

A Monte Carlo simulation is performed with the optical properties of the calibration sample. The simulation is then divided by the experimental reflectance performed on the calibration sample. The result, that must be independent of the source-detector separation, is defined as the calibration factor. Each new measurement can be multiplied by the calibration factor.